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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,346	03/06/2003	Joanne Elizabeth Burn	50341-041	3207

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McDermott Will & Emery
600 13th Street NW
Washington, DC 20005-3096

EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,346	BURN ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *4,5,13 and 17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/4/01 & 12/12/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/4/01, 6/9/03*. 1/22/03, P/22/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence search result*.

DETAILED ACTION

1. Claims 1-22 are pending.

2. Applicant's election with traverse of Group I, claims 1-3, 6-9, 12 and 14-16 including SEQ ID NO:2 in the reply filed on 5/4/2006 is acknowledged. The traversal is on the ground(s) that the claims of Group I and IV are so linked that they form a single general inventive concept (page 1 of Response, 3rd paragraph).

Group I and IV have been rejoined.

Applicants contend that SEQ ID NO:1 should be included in the present application because SEQ ID NO:1 and 2 are related as genomic and cDNA sequences (page 2 of Response, 1st full paragraph).

This is not found persuasive because the Office contends that the structure and function of SEQ ID NO:1 has not been defined. Applicants only state that it is a genomic sequence but do not disclose, for example, the coding region. The Office contends that Applicants disclose an Arabidopsis FLF genomic sequence in NCBI accession number AF116528, and this sequence is 6051 base pairs in length (See Sheldon et al 1999, The Plant Cell 11:445-458, page 450, right column, 5th line). Applicants' SEQ ID NO:1 is 7968 base pairs in length. The Office contends that the additional base pairs as well as the 5' and 3' untranslated regions and introns have a separate activity that is not found in the cDNA sequence of SEQ ID NO:2.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4-5, 13 and 17-22 are withdrawn from consideration for being drawn to non-elected inventions.

3. Claims 1-3, 6-12 and 14-16, including SEQ ID NO:2 are examined in the present office action.

4. For purposes of examination, Applicant is reminded of the petition decision filed 17 September 2004, in which the date under 35 U.S.C. 371 (c)(1), (2) and (4) is 06 March 2003.

Specification

5. Objection is made to the specification for not incorporating SEQ ID NO's when referring to nucleic acid or amino acid sequences. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: X) in all instances where the description or claims of a patent application discuss sequences. In the instant Application, Figure 9 discloses a DNA and amino acid sequence and Figure 10 discloses two amino acid sequences. The Brief Description of the Drawings can be amended to include the sequence identifiers.

Information Disclosure Statement

6. The information disclosure statement filed 1/22/2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, **date**, and place of publication. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the

statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objection

7. Claims 1-2, 6-12 and 15-16 are objected to for being drawn to non-elected inventions. Correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14 and 15 are indefinite in the recitation "FLF gene". The sole designation of a nucleic acid sequence by "FLF gene" is arbitrary and creates ambiguity in the claims. For example, the nucleic acid sequence in this application could be designated by some other arbitrary means, or the assignment of said name could be arbitrarily changed to designate a different nucleic acid sequence. If either event occurs, one's ability to determine the metes and bounds of the claim would be impaired. See *In re Hammack*, 427 F .2d 1378, 1382; 166 USPQ 204, 208 (CCPA 1970). Amendment of the claim to refer to a specific SEQ ID NO would obviate this rejection.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 6-12 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule comprising a MADS box and which comprises a nucleic acid molecule capable of hybridizing to SEQ ID NO:2 other than to the MADS box region under at least low stringency hybridization conditions, or which comprises a nucleic acid molecule which has at least 70% sequence identity outside the MADS box region of SEQ ID NO:2, or comprising a nucleic acid molecule which hybridizes under stringent conditions to SEQ ID NO:2, or has at least 80% sequence identity to SEQ ID NO:2, or wherein said nucleic acid molecule comprises a nucleotide sequence corresponding to a FLOWERING LOCUS F (FLF) gene or a biologically active fragment thereof; a vector, plant cell or transformed plant comprising said nucleic acid molecule; a method of isolating a nucleic acid molecule comprising a previously recited nucleic acid molecule; or a method of delaying flowering in a plant comprising said nucleic acid molecule; or a method of modifying the vegetative and/or floral phenotype of a plant or modifying the response of a plant to vernalisation comprising increasing the level of expression of an FLF gene, or wherein the FLF gene comprises a previously recited nucleic acid molecule.

Applicants isolated their invention by transposon tagging Arabidopsis thaliana ecotype C24 plants. Mutant plants were screened for those that exhibited a delay in flower initiation. Applicants designated the mutant locus FLOWERING LOCUS F (FLF) (page 18, lines 10-30). Applicants isolated the corresponding cDNA sequence using as a probe DNA sequences that were on either side of the T-DNA insertion (page 21-22, Example 4). Applicants disclose the cDNA sequence as SEQ ID NO:2 (sequence listing and page 2 of Response to Restriction, 1st full paragraph). Applicant discloses no homologous sequences were found (page 22, top sentence).

The Applicants do not identify essential regions of the FLF protein encoded by SEQ ID NO:2, nor do Applicants describe any polynucleotide sequences that hybridize to SEQ ID NO:2 under low stringency conditions, wherein hybridization occurs outside the MADS box region and encode a functional FLF protein.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the

genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a FLF protein falling within the scope of the claimed genus of polynucleotides which hybridize under low stringency conditions to SEQ ID NO:2 or which exhibit 70% sequence identity outside the MADS box region of SEQ ID NO:2 or are biologically active fragments thereof. Applicants only describe a single cDNA sequence of SEQ ID NO:2. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the FLF protein encoded by SEQ ID NO:2, it remains unclear what features identify an Arabidopsis FLF protein. Since the genus of FLF proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

10. Claims 1-2, 6-12 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising SEQ ID NO:2 and an Arabidopsis thaliana ecotype erecta plant transformed with said nucleic acid molecule wherein the nucleic acid molecule is in sense orientation, and method for delaying flowering in Arabidopsis thaliana ecotype erecta comprising transforming said plant with a nucleic acid molecule comprising SEQ ID NO:2 in sense orientation, does not reasonably provide enablement

for a nucleic acid molecule capable of hybridizing to SEQ ID NO:2 other than to the MADS box region under at least low stringency hybridization conditions, or which comprises a nucleic acid molecule which has at least 70% sequence identity outside the MADS box region of SEQ ID NO:2, or comprising a nucleic acid molecule which hybridizes under stringent conditions to SEQ ID NO:2, or has at least 80% sequence identity to SEQ ID NO:2, or wherein said nucleic acid molecule comprises a nucleotide sequence corresponding to a FLOWERING LOCUS F (FLF) gene or a biologically active fragment thereof; a vector, plant cell or transformed plant comprising said nucleic acid molecule; a method of isolating a nucleic acid molecule comprising a previously recited nucleic acid molecule; or a method of delaying flowering in a plant comprising said nucleic acid molecule; or a method of modifying the vegetative and/or floral phenotype of a plant or modifying the response of a plant to vernalisation comprising increasing the level of expression of an FLF gene, or wherein the FLF gene comprises a previously recited nucleic acid molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid molecule comprising a MADS box and which comprises a nucleic acid molecule capable of hybridizing to SEQ ID NO:2 other than to the MADS box region under at least low stringency hybridization conditions, or which comprises a nucleic acid molecule which has at least 70% sequence identity outside the MADS box region of SEQ ID NO:2, or comprising a nucleic acid molecule which hybridizes under stringent conditions to SEQ ID NO:2, or has at least 80% sequence identity to SEQ ID NO:2, or wherein said nucleic acid molecule comprises a nucleotide sequence corresponding to a FLOWERING LOCUS F (FLF) gene or a biologically active fragment thereof; a vector, plant cell or transformed plant comprising said nucleic acid molecule; a method of isolating a nucleic acid molecule comprising a previously recited nucleic acid molecule or a functional portion thereof; or a method of delaying flowering in a plant comprising said nucleic acid molecule; or a method of modifying the vegetative and/or floral phenotype of a plant or modifying the response of a plant to vernalisation comprising increasing the level of expression of an FLF gene, or wherein the FLF gene comprises a previously recited nucleic acid molecule.

Applicants isolated their invention by transposon tagging Arabidopsis thaliana ecotype C24 plants. Mutant plants were screened for those that exhibited a delay in flower initiation. Applicants designated the mutant locus FLOWERING LOCUS F (FLF) (page 18, lines 10-30). Applicants isolated the corresponding cDNA sequence using as a probe DNA sequences that were on either side of the T-DNA insertion (page 21-22, Example 4). Applicants disclose the cDNA sequence as SEQ ID NO:2 (sequence listing and page 2 of Response to Restriction, 1st

full paragraph). Applicant discloses a search of the protein sequence yielded no homologous sequences were found (page 22, top sentence). Applicants disclose Arabidopsis thaliana ecotype Landsberg erecta overexpressing SEQ ID NO:2 (FLF) causes a delay in flowering time, whereas in C24 it causes either a delay in flowering, or causes the plants to flower significantly earlier (page 30, lines 3-12).

The state-of-the-art teaches that flowering time control in plants is a complicated process that involves the integration of multiple signals and pathways. MacDonald et al (2003, Cell 113:671-672) teach that there are four distinct pathways that control flowering in Arabidopsis (page 671, left column, 2nd paragraph). In addition, Applicants own admitted statement (see above) that transforming two different ecotypes of Arabidopsis produced opposite phenotypes attests to the complexity of flowering not only between different species of plant but also between two separate ecotypes of the same species of plant. Shin et al (2003, Journal of Plant Biology 46(1):46-51) disclose tobacco transformed with OsMADS1, a rice MADS box gene, cause unexpected results of reduced apical dominance, dwarfism and early flowering, as well as flowers which contained a homeotic replacement of the carpel organ with one or more flowers (page 48, right column, "Homeotic Mutation of Floral Organs").

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that are 70% identical outside the MADS box region of SEQ ID NO:2 will encode a protein with the same activity as a protein encoded by SEQ ID NO:2. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of

maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

Re: claims 14 and 15 recite increasing the level of expression of an FLF gene. A method of increasing the level of expression of any gene encompasses not only overexpressing said gene using a construct comprising said gene operably linked to any promoter, but also includes for example, overexpressing enhancers of said gene or repressing repressors of said gene. Applicants are not enabled for claims broadly reciting "increasing the level of expression of an FLF gene".

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 or 3 as probes or by designing primers to undisclosed regions of SEQ ID NO:1 or 3 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to

identify those, if any, that when over-expressed have diacylglycerol acyltransferase activity and exhibit 90% identity with SEQ ID NO:1 or 3.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-2, 6-12 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Sheldon et al (1999, The Plant Cell 11:445-458; listed in IDS).

The claims are drawn to an isolated nucleic acid molecule comprising a MADS box and which comprises the nucleotide sequence set forth in SEQ ID NO:2, or which comprises a nucleic acid molecule capable of hybridizing to SEQ ID NO:2 other than to the MADS box region under at least low stringency hybridization conditions, or which comprises a nucleic acid molecule which has at least 70% sequence identity outside the MADS box region of SEQ ID NO:2, or comprising a nucleic acid molecule which hybridizes under stringent conditions to SEQ ID NO:2, or has at least 80% sequence identity to SEQ ID NO:2, or wherein said nucleic acid molecule comprises a nucleotide sequence corresponding to a FLOWERING LOCUS F (FLF) gene or a biologically active fragment thereof; a vector, plant cell or transformed plant comprising said nucleic acid molecule; a method of isolating a nucleic acid molecule comprising a previously recited nucleic acid molecule or a functional portion thereof; or a method of delaying flowering in a plant comprising said nucleic acid molecule; or a method of modifying

the vegetative and/or floral phenotype of a plant or modifying the response of a plant to vernalisation comprising increasing the level of expression of an FLF gene, or wherein the FLF gene comprises a previously recited nucleic acid molecule.

Sheldon et al disclose a nucleic acid molecule exhibiting 100% sequence identity with SEQ ID NO:2 (see page 450, right column, 4th line from the top and enclosed sequence search results), wherein expression of said nucleic acid molecule in sense orientation, in an Arabidopsis plant, delays flowering in said plant (page 449, right column, 1st full paragraph). Sheldon et al disclose said nucleic acid molecule in a vector (paragraph bridging pages 456 and 457). Sheldon et al disclose a method for isolating said nucleic acid molecule using a 2.7 kb fragment of DNA which comprises a functional portion of Applicants' SEQ ID NO:2 and is capable of hybridizing to SEQ ID NO:2 under at least low stringency conditions (page 456, "Screening of cDNA Libraries") and Sheldon et al increase the level of expression of an FLF gene (page 449, right column, "Transgenic Plants Overexpressing FLF Have Altered Flowering Times"), and as such, Sheldon et al anticipate the claimed invention.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
June 2, 2006

STUART F. BAUM, PH.D.
PATENT EXAMINER